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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,343	11/01/2005	Akira Kato	1089.0590000/MAC	4524

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EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
1628	

MAIL DATE	DELIVERY MODE
09/30/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/555,343	KATO ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-18,21-23 and 28-43* is/are pending in the application.

4a) Of the above claim(s) *16-18 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendments filed 7/21/2010 were entered.

Response to Arguments

2. Applicants' arguments, filed 7/21/2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. **Instant claims 28-43 are rejected rejected under 35 U.S.C. 103(a) as being unpatentable over *Miyake et al* (cited in a previous Action) in view of *Driskell* (cited in a previous Action)**.

6. Instant claim 28 is drawn to a freeze-dried preparation comprising methylcobalamin or a pharmacologically and an excipient, wherein said excipient comprises at least one sugar (selected from glucose, fructose, maltose, lactose, sucrose and trehalose) in an amorphous state. More specifically, the amorphous sugar is present in an amount of at least 20% by weight, based on the total weight of the excipient, as recited by instant claim 29. Additionally, as recited by instant claim 30, the freeze-dried preparation further comprises a pH adjuster and, as recited by instant claim 31, further comprises an anti-oxidant. Moreover, as recited by instant claim 33, the methylcobalamin is also in an amorphous state. As thus summarized, the invention reads on claims 28-36.

7. As discussed in the previous Action mailed on 3/29/2010, *Miyake et al* disclose a preparation comprising vitamin B_{12} (10 μg), lactose (50 μg), an antioxidant (Vitamin E (10 mg)), and a pH adjuster (NaOH) which is then freeze-dried (Pages 8-9, Practical Example 1). More specifically, *Miyake et al* refer to Vitamin B_{12} as "cyanocobalamine" (Page 6, Table 1). However, as discussed in the previous Action and acknowledged by Applicant, methylcobalamin is the active form of vitamin B_{12} (as evidenced by *Driskell* (Page 75); see also Applicant Arguments, Page 9). Accordingly, as discussed in the previous Action, the ordinarily skilled artisan would have found it *prima facie* obvious to replace cyanocobalamin in the formulation taught by *Miyake et al* with methylcobalamin in view of *Diskell*. The skilled artisan would have been motivated to formulate the vitamin preparation comprising vitamin B_{12} taught by *Miyake et*

al using methylcobalamin in view of *Diskell*, who teaches that methylcobalamin (not cyanocobalamin) is the active form of vitamin B_{12}.

8. As such, *Miyake et al* in view of *Driskell* disclose a freeze-dried preparation comprising methylcobalamin and an excipient (i.e., lactose). Although *Miyake et al* do not specifically disclose that the lactose in the freeze-dried preparation is amorphous or that the methylcobalamin in the freeze-dried preparation is amorphous, it is asserted – absent evidence to the contrary – that the lactose and methylcobalamin would necessarily be in an amorphous state in the freeze-dried preparation taught by *Miyake et al* in view of *Driskell*. As stated in *In re Best, Bolton, and Shaw*, "Where… the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product" 195 USPQ 430, 433, 562 F2d 1252 (CCPA 1977). In the instant case, the claimed and prior art products are substantially identical. Accordingly, it is asserted that the prior art freeze-dried product would necessarily comprising amorphous lactose and amorphous methylcobalamin, absent evidence to the contrary. See also *In re Fitzgerald* 205 USPQ 594, 597, 619 F2d 67 (CCPA 1980): the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on.

9. As such, instant claims 28-36 are rejected as *prima facie* obvious.

10. Applicant traverses the above rejection on a variety of grounds. First, Applicant argues that cyanocobalamin and methylcobalamin are distinct agents (Applicant Argument, Page 9). Applicant's argument as to this point is considered persuasive. However, as indicated above and discussed in the previous Action, the skilled artisan would have been motivated to formulate the

vitamin preparation comprising vitamin B_{12} taught by *Miyake et al* using methylcobalamin in view of *Diskell*, who teaches that methylcobalamin (not cyanocobalamin) is the active form of vitamin B_{12}. Yet, Applicant argues that said replacement of cyanocobalamin with methylcobalamin would not have been obvious. In particular, Applicant notes that whereas cyanocobalamin is photostable in the presence of mannitol (i.e., excipient), methylcobalamin is not (Applicant Argument, Pages 9-13; see also Affidavits filed 7/21/2010 comprising Exhibits 1-3). In view of the discrepancy in photostability between methylcobalamin and cyanocobalamin, Applicant argues it would not have been motivated to substitute the less stable agent (methylcobalamin) in place of the more stable agent (cyanocobalamin). However, as noted by Applicant, methylcobalamin is subject to photodegradation when it is kept in a brown ampule ***without a light-protect easy open pack*** (Applicant Argument, Page 11). It is asserted that it would have been within the skill of the ordinary artisan at the time to package the prima facie obvious invention in a light–protect easy open pack. Furthermore, it is significant that the Exhibits cited by Applicant (which demonstrate a lack of photostability of methylcobalamin in mannitol without a light-protect easy open pack) disclose non-lyophilized solutions. Conversely, the freeze-dried preparation of *Miyake et al* is described as having good stability (Page 5). Since the skilled artisan would have reasonably believed that said stability is due in part to formulating the preparation in a freeze-dried state, the fact that methylcobalamin is less photo-stable than cyanocobalamin would not have deterred the substitution. For either of these reasons it is not considered persuasive that the skilled artisan would not have substituted methylcobalamin in place of cyanocobalamin in the preparation taught by *Miyake et al* with a reasonable expectation of success.

11. Applicant next argues that *Miyake et al* is directed to a problem that is unique to multivitamin preparations that contain at least one fat-soluble vitamin: "Miyake only adds the excipient… to compensate for the presence of a surface active agent, and the surface active agent is only desired because of the fat soluble vitamins that are present" (Applicant Arguments, Pages 13-16). However, the *prima facie* obvious modification of *Miyake et al* in view of *Diskell* (i.e., substituting methylcobalamin in place of cyanocobalamin as Vitamin B_{12} in a preparation comprising vitamin B_{12} (10 μg), lactose (50 μg), an antioxidant (Vitamin E (10 mg)), and a pH adjuster (NaOH) which is then freeze-dried (Pages 8-9, Practical Example 1)) provides a multivitamin preparation that also contains at least one fat-soluble vitamin (e.g., vitamin A (see Table 1, Page 6)) in addition to methylcobalamin. Since the instant claims do not exclude such ingredients, it is not persuasive that the substitution would "fundamentally alter the principle operation of the preparation of Miyake" (Applicant Argument, Page 15).

12. Lastly, Applicant argues that lyophilization of the preparation as disclosed by *Miyake et al* does not require production of an amorphous state as recited by the instant claims, noting that mannitol can be present in crystalline and/or amorphous forms depending on the conditions during the freeze drying procedure (Applicant Argument, Page 16). However, the prima facie obvious preparation does not comprising mannitol as an excipient. Rather, as discussed above, the preparation comprises lactose. Thus, as previously discussed, *Miyake et al* in view of *Driskell* disclose a freeze-dried preparation comprising methylcobalamin and an excipient (i.e., lactose). Although *Miyake et al* do not specifically disclose that the lactose in the freeze-dried preparation is amorphous or that the methylcobalamin in the freeze-dried preparation is amorphous, it is asserted – absent evidence to the contrary – that the lactose and

methylcobalamin would necessarily be in an amorphous state in the freeze-dried preparation taught by *Miyake et al* in view of *Driskell*. As stated in *In re Best, Bolton, and Shaw*, "Where… the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product" 195 USPQ 430, 433, 562 F2d 1252 (CCPA 1977). In the instant case, the claimed and prior art products are substantially identical. Accordingly, it is asserted that the prior art freeze-dried product would necessarily comprising amorphous lactose and amorphous methylcobalamin, absent evidence to the contrary. See also *In re Fitzgerald* 205 USPQ 594, 597, 619 F2d 67 (CCPA 1980): the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on". Since Applicant has not introduced any evidence to meet their burden, the argument is not considered persuasive.

13. Thus, for all the foregoing reasons, Applicant's arguments are not considered persuasive. The rejection of claims 28-36 is maintained.

14. In the previous Action, instant claims 37-43 were also rejected as prima facie obvious. Since Applicant does not specifically traverse the rejection of claims 37-43 beyond the arguments discussed above and not considered persuasive, the rejection of claims (reiterated as follows) is maintained:

15. Instant claims 37-43 are all drawn to a freeze dried preparation comprising methylcobalamin and an excipient wherein the freeze dried preparation is obtained by a specific

PRODUCT-BY-PROCESS CLAIMS ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted)

process. As stated by MPEP 2113: . In the instant case, the instantly claimed product in the product-by-process claim is obvious from a product of the prior art as previously discussed in view of *Mayake et al* in view of *Driskell*. Accordingly, the obvious product as obtained by the process recited by claims 37-43 is rejected as *prima facie* obvious.

Conclusion

No new ground(s) of rejection are presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1628

/Brandon J Fetterolf/
Supervisory Patent Examiner, Art Unit 1628